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STRUCTURE FILE UPDATES: 20 MAR 2008 HIGHEST RN 1009361-91-4
DICTIONARY FILE UPDATES: 20 MAR 2008 HIGHEST RN 1009361-91-4

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TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

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predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stdnoc/properties.html>

=>

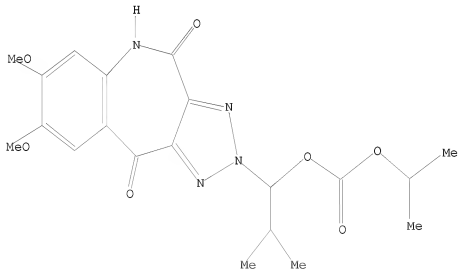
Uploading C:\Program Files\Stnexp\Queries\10561212.str

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1 exact

SAMPLE SEARCH INITIATED 16:39:31 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 1 TO ITERATE

100.0% PROCESSED 1 ITERATIONS 0 ANSWERS
 SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
 BATCH **COMPLETE**

PROJECTED ITERATIONS: 1 TO 80
 PROJECTED ANSWERS: 0 TO 0

L2 0 SEA EXA SAM L1

=> s l1 sss sam
 SAMPLE SEARCH INITIATED 16:39:49 FILE 'REGISTRY'
 SAMPLE SCREEN SEARCH COMPLETED - 1 TO ITERATE

100.0% PROCESSED 1 ITERATIONS 0 ANSWERS
 SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
 BATCH **COMPLETE**

PROJECTED ITERATIONS: 1 TO 80
 PROJECTED ANSWERS: 0 TO 0

L3 0 SEA SSS SAM L1

=> file caplus
 COST IN U.S. DOLLARS

| | SINCE FILE ENTRY | TOTAL SESSION |
|---------------------|------------------|---------------|
| FULL ESTIMATED COST | 0.92 | 1.13 |

FILE 'CAPLUS' ENTERED AT 16:40:12 ON 21 MAR 2008
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FILE COVERS 1907 - 21 Mar 2008 VOL 148 ISS 13
 FILE LAST UPDATED: 20 Mar 2008 (20080320/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/infopolicy.html>

=> s ?benzazepine
 L4 3243 ?BENZAZEPINE

=> s l4 and triazolo
 7589 TRIAZOLO
 L5 29 L4 AND TRIAZOLO

=> s 15 and cellulose
 365509 CELLULOSE
 4460 CELLULOSES
 366018 CELLULOSE
 (CELLULOSE OR CELLULOSES)
 L6 2 L5 AND CELLULOSE

=> dis 16 1-2 bib abs

L6 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2004:1154779 CAPLUS
 DN 142:62766
 TI Product of coprecipitation of sparingly soluble substance and
 water-soluble polymer and process for producing the same
 IN Ishikura, Toyooki; Udagawa, Chikako; Misaka, Masato; Suemune, Kenji;
 Kitahara, Shinichi; Ono, Kiyoko; Koyanagi, Akihiro
 PA Meiji Seika Kaisha, Ltd., Japan
 SO PCT Int. Appl., 31 pp.
 CODEN: PIXXD2
 DT Patent
 LA Japanese
 FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| PI | WO 2004113451 | A1 | 20041229 | WO 2004-JP8727 | 20040621 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | EP 1650266 | A1 | 20060426 | EP 2004-746196 | 20040621 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |
| | US 2007167402 | A1 | 20070719 | | 20051219 |
| | US 2003-175646 | A | 20030620 | US 2005-561212 | |
| PRAI | WO 2004-JP8727 | W | 20040621 | | |

AB Disclosed is a product of the copptn. of 2-(1-isopropoxy-carbonyloxy-2-methylpropyl)-7,8-dimethoxy-4(5H),10-dioxo-2H-1,2,3-triazolo [4,5-c][1]benzoazepine (I) and a water-soluble polymer. The copptn. product is excellent in solubility and absorbability. Crystalline I and Me cellulose were dissolved in DMSO. The mixture was dropped into an aqueous solution containing Me cellulose to give ppts., which showed a solubility 16.8 µg/mL, as compared to 0.8 µg/mL for crystalline I.

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2003:532667 CAPLUS
 DN 139:90493
 TI Amorphous substance of tricyclic triazolobenzazepine derivative
 IN Ishikura, Toyooki; Ishizawa, Takayuki; Suemune, Kenji; Ishiwata, Mayumi;
 Udagawa, Chikako
 PA Meiji Seika Kaisha, Ltd., Japan
 SO PCT Int. Appl., 25 pp.

CODEN: PIXXD2
 DT Patent
 LA Japanese
 FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-----------|---|------|----------|-----------------|----------|
| PI | WO 2003055886 | A1 | 20030710 | WO 2002-JP13558 | 20021225 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2471651 | A1 | 20030710 | CA 2002-2471651 | 20021225 |
| | AU 2002367110 | A1 | 20030715 | AU 2002-367110 | 20021225 |
| | EP 1466914 | A1 | 20041013 | EP 2002-790871 | 20021225 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| | CN 1617872 | A | 20050518 | CN 2002-827547 | 20021225 |
| | US 2005130955 | A1 | 20050616 | US 2004-500071 | 20040625 |
| | US 7229985 | B2 | 20070612 | | |
| PRAI | JP 2001-393016 | A | 20011226 | | |
| | WO 2002-JP13558 | W | 20021225 | | |
| AB | Disclosed are amorphous 2-(1-isopropoxycarbonyloxy-2-methylpropyl)-7,8-dimethoxy-4(5H),10-dioxo-2H-1,2,3-triazolo[4,5-c][1]benzazepine (I), which is improved in absorbability and solubility; and a medicinal composition containing the compound Also provided are processes for producing amorphous compound I and for producing a medicinal composition containing the compound An amorphous compound I was dissolved in methylene chloride, and mixed with Me cellulose (Metolose SM15) and methanol. The mixture was then spray dried to obtain an amorphous powder of the present invention. | | | | |
| RE.CNT 11 | THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT | | | | |

=> s 15 and coprecip?
 6863 COPRECIP?
 2591 COPPT
 1482 COPPTS
 3609 COPPT
 (COPPT OR COPPTS)
 6440 COPPTD
 1034 COPPTG
 17317 COPPTN
 61 COPPTNS
 17339 COPPTN
 (COPPTN OR COPPTNS)
 25841 COPRECIP?
 (COPRECIP? OR COPPT OR COPPTD OR COPPTG OR COPPTN)
 L7 1 L5 AND COPRECIP?

=> dis 17 bib abs

L7 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2004:1154779 CAPLUS

DN 142:62766

TI Product of coprecipitation of sparingly soluble substance and water-soluble polymer and process for producing the same

IN Ishikura, Toyooki; Udagawa, Chikako; Misaka, Masato; Suemune, Kenji; Kitahara, Shinichi; Ono, Kiyoko; Koyanagi, Akihiro

PA Meiji Seika Kaisha, Ltd., Japan

SO PCT Int. Appl., 31 pp.

CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|----------------|--|----------|-----------------|----------|
| PI | WO 2004113451 | A1 | 20041229 | WO 2004-JP8727 | 20040621 |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| | RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| | EP 1650266 | A1 | 20060426 | EP 2004-746196 | 20040621 |
| | R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | |
| | US 2007167402 | A1 | 20070719 | US 2005-561212 | 20051219 |
| PRAI | JP 2003-175646 | A | 20030620 | | |
| | WO 2004-JP8727 | W | 20040621 | | |

AB Disclosed is a product of the copptn. of 2-(1-isopropoxy-carbonyloxy-2-methylpropyl)-7,8-dimethoxy-4(5H),10-dioxo-2H-1,2,3-triazolo[4,5-c][1]benzazepine (I) and a water-soluble polymer. The copptn. product is excellent in solubility and absorbability. Crystalline I and Me cellulose were dissolved in DMSO. The mixture was dropped into an aqueous solution containing Me cellulose to give ppts., which showed a solubility 16.8

µg/mL, as compared to 0.8 µg/mL for crystalline I.

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s 15 and allerg?

77230 ALLERG?

L8 3 L5 AND ALLERG?

=> dis 18 1-3 bib abs

L8 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2004:1154779 CAPLUS

DN 142:62766

TI Product of coprecipitation of sparingly soluble substance and water-soluble polymer and process for producing the same

IN Ishikura, Toyooki; Udagawa, Chikako; Misaka, Masato; Suemune, Kenji; Kitahara, Shinichi; Ono, Kiyoko; Koyanagi, Akihiro

PA Meiji Seika Kaisha, Ltd., Japan

SO PCT Int. Appl., 31 pp.

CODEN: PIXXD2

DT Patent

LA Japanese
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--------|---|------|----------|-----------------|----------|
| PI | WO 2004113451 | A1 | 20041229 | WO 2004-JP8727 | 20040621 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | EP 1650266 | A1 | 20060426 | EP 2004-746196 | 20040621 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |
| | US 2007167402 | A1 | 20070719 | US 2005-561212 | 20051219 |
| | JP 2003-175646 | A | 20030620 | | |
| | WO 2004-JP8727 | W | 20040621 | | |
| AB | Disclosed is a product of the copptn. of 2-(1-isopropoxy-carbonyloxy-2-methylpropyl)-7,8-dimethoxy-4(5H),10-dioxo-2H-1,2,3-triazolo [4,5-c][1]benzazepine (I) and a water-soluble polymer. The copptn. product is excellent in solubility and absorbability. Crystalline I and Me cellulose were dissolved in DMSO. The mixture was dropped into an aqueous solution containing Me cellulose to give ppts., which showed a solubility 16.8 µg/mL, as compared to 0.8 µg/mL for crystalline I. | | | | |
| RE.CNT | 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT | | | | |

L8 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2004:1154716 CAPLUS

DN 142:100324

TI Tricyclic triazolobenzazepine derivative produced as novel crystalline substance

IN Kitahara, Shinichi; Yamaguchi, Toshihiro

PA Meiji Seika Kaisha, Ltd., Japan

SO PCT Int. Appl., 21 pp.

CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---|------|----------|-----------------|----------|
| PI | WO 2004113343 | A1 | 20041229 | WO 2004-JP8729 | 20040621 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | EP 1642900 | A1 | 20060405 | EP 2004-746198 | 20040621 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
 US 2007167432 A1 20070719 US 2005-561211 20051219
 PRAI JP 2003-175347 A 20030619
 WO 2004-JP8729 W 20040621
 AB Crystalline 2-(1-isopropoxycarbonyloxy-2-methylpropyl)-7,8-dimethoxy-4(5-H),10-
 dioxo-2H-1,2,3-triazolo[4,5-c][1]benzazepine (I) (X
 ray crystallog. data given) is claimed. The crystals of I of this
 invention have high solubility and bioavailability. Crystallization of I from
 DMF and
 water gave β type crystals of I. I is an antiallergic agent.
 RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2008 ACS on SIN
 AN 2003:532666 CAPLUS
 DN 139:95490
 TI Crystalline tricyclic triazolobenzazepine derivative
 IN Kitahara, Shin-Ichi; Furukawa, Hanae; Yamaguchi, Toshihiro; Miyamoto,
 Sachiko; Okada, Yumiko
 PA Meiji Seika Kaisha, Ltd., Japan
 SO PCT Int. Appl., 17 pp.
 CODEN: PIXXD2
 DT Patent
 LA Japanese
 FAN.CNT 2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| PI WO 2003055885 | A1 | 20030710 | WO 2002-JP13557 | 20021225 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2002367109 | A1 | 20030715 | AU 2002-367109 | 20021225 |
| EP 1469000 | A1 | 20041020 | EP 2002-790870 | 20021225 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| CN 1617872 | A | 20050518 | CN 2002-827547 | 20021225 |
| US 2005020579 | A1 | 20050127 | US 2004-500157 | 20040625 |
| US 7002009 | B2 | 20060221 | | |
| PRAI JP 2001-393016 | A | 20011226 | | |
| WO 2002-JP13557 | W | 20021225 | | |
| AB Crystalline 2-(1-isopropoxycarbonyloxy-2-methylpropyl)-7,8-dimethoxy-4(5-H),10- dioxo-2H-1,2,3-triazolo[4,5-c][1]benzazepine (I) (X ray crystallog. data given) is claimed. I is an antiallergic agent. RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT | | | | |

=> s 15 and polymer
 1184051 POLYMER
 943758 POLYMERS
 1583621 POLYMER
 (POLYMER OR POLYMERS)
 L9 2 L5 AND POLYMER

=> dis 19 1-2 bib abs

L9 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2008 ACS on SIN
 AN 2004:1154779 CAPLUS
 DN 142:62766
 TI Product of coprecipitation of sparingly soluble substance and
 water-soluble polymer and process for producing the same
 IN Ishikura, Toyooki; Udagawa, Chikako; Misaka, Masato; Suemune, Kenji;
 Kitahara, Shinichi; Ono, Kiyoko; Koyanagi, Akihiro
 PA Meiji Seika Kaisha, Ltd., Japan
 SO PCT Int. Appl., 31 pp.
 CODEN: PIXXD2
 DT Patent
 LA Japanese
 FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--------|--|---|----------|-----------------|----------|
| PI | WO 2004113451 | A1 | 20041229 | WO 2004-JP8727 | 20040621 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SI, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | EP 1650266 | A1 | 20060426 | EP 2004-746196 | 20040621 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |
| | US 2007167402 | A1 | 20070719 | US 2005-561212 | 20051219 |
| PRAI | JP 2003-175646 | A | 20030620 | | |
| | WO 2004-JP8727 | W | 20040621 | | |
| AB | Disclosed is a product of the copptn. of 2-(1-isopropoxy-carbonyloxy-2-methylpropyl)-7,8-dimethoxy-4(5H),10-dioxo-2H-1,2,3-triazolo [4,5-c][1]benzoozepine (I) and a water-soluble polymer. The copptn. product is excellent in solubility and absorbability. Crystalline I and Me cellulose were dissolved in DMSO. The mixture was dropped into an aqueous solution containing Me cellulose to give ppts., which showed a solubility 16.8 µg/mL, as compared to 0.8 µg/mL for crystalline I. | | | | |
| RE.CNT | 15 | THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT | | | |

L9 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2008 ACS on SIN
 AN 2003:532667 CAPLUS
 DN 139:90493
 TI Amorphous substance of tricyclic triazolobenzazepine derivative
 IN Ishikura, Toyooki; Ishizawa, Takayuki; Suemune, Kenji; Ishiwata, Mayumi;
 Udagawa, Chikako
 PA Meiji Seika Kaisha, Ltd., Japan
 SO PCT Int. Appl., 25 pp.
 CODEN: PIXXD2
 DT Patent
 LA Japanese
 FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|-----------------|--|----------|-----------------|----------|
| PI | WO 2003055886 | A1 | 20030710 | WO 2002-JP13558 | 20021225 |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| | RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| | CA 2471651 | A1 | 20030710 | CA 2002-2471651 | 20021225 |
| | AU 2002367110 | A1 | 20030715 | AU 2002-367110 | 20021225 |
| | EP 1466914 | A1 | 20041013 | EP 2002-790871 | 20021225 |
| | R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | |
| | CN 1617872 | A | 20050518 | CN 2002-827547 | 20021225 |
| | US 2005130955 | A1 | 20050616 | US 2004-500071 | 20040625 |
| | US 7229985 | B2 | 20070612 | | |
| PRAI | JP 2001-393016 | A | 20011226 | | |
| | WO 2002-JP13558 | W | 20021225 | | |

AB Disclosed are amorphous 2-(1-isopropoxycarbonyloxy-2-methylpropyl)-7,8-dimethoxy-4(5H),10-dioxo-2H-1,2,3-triazolo[4,5-c][1] benzazepine (I), which is improved in absorbability and solubility; and a medicinal composition containing the compound Also provided are processes for producing amorphous compound I and for producing a medicinal composition containing the compound An amorphous compound I was dissolved in methylene chloride, and mixed with Me cellulose (Metolose SM15) and methanol. The mixture was then spray dried to obtain an amorphous powder of the present invention.

RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s Ishikura Toyoaki/AU
L10 29 ISHIKURA TOYOAKI/AU

=> s l10 and benzazepine
2261 BENZAZEPINE
774 BENZAZEPINES
2471 BENZAZEPINE
(BENZAZEPINE OR BENZAZEPINES)

L11 1 L10 AND BENZAZEPINE

=> dis l11 bib abs

L11 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2003:532667 CAPLUS
DN 139:90493
TI Amorphous substance of tricyclic triazolobenzazepine derivative
IN Ishikura, Toyoaki; Ishizawa, Takayuki; Suemune, Kenji; Ishiwata, Mayumi; Udagawa, Chikako
PA Meiji Seika Kaisha, Ltd., Japan
SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|-----------------|--|----------|-----------------|----------|
| PI | WO 2003055886 | A1 | 20030710 | WO 2002-JP13558 | 20021225 |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| | RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| | CA 2471651 | A1 | 20030710 | CA 2002-2471651 | 20021225 |
| | AU 2002367110 | A1 | 20030715 | AU 2002-367110 | 20021225 |
| | EP 1466914 | A1 | 20041013 | EP 2002-790871 | 20021225 |
| | R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | |
| | CN 1617872 | A | 20050518 | CN 2002-827547 | 20021225 |
| | US 2005130955 | A1 | 20050616 | US 2004-500071 | 20040625 |
| | US 7229985 | B2 | 20070612 | | |
| PRAI | JP 2001-393016 | A | 20011226 | | |
| | WO 2002-JP13558 | W | 20021225 | | |

AB Disclosed are amorphous 2-(1-isopropoxycarbonyloxy-2-methylpropyl)-7,8-dimethoxy-4(5H),10-dioxo-2H-1,2,3-triazolo[4,5-c][1]benzazepine (I), which is improved in absorbability and solubility; and a medicinal composition containing the compound. Also provided are processes for producing amorphous compound I and for producing a medicinal composition containing the compound.

An amorphous compound I was dissolved in methylene chloride, and mixed with Me cellulose (Metolose SM15) and methanol. The mixture was then spray dried to obtain an amorphous powder of the present invention.

RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s 110 and coprecip?
6863 COPRECIP?
2591 COPPT
1482 COPPTS
3609 COPPT
(COPPT OR COPPTS)
6440 COPPTD
1034 COPPTG
17317 COPPTN
61 COPPTNS
17339 COPPTN
(COPPTN OR COPPTNS)
25841 COPRECIP?
(COPRECIP? OR COPPT OR COPPTD OR COPPTG OR COPPTN)

L12 2 L10 AND COPRECIP?

=> dis l12 1-2 bib abs

L12 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:1154779 CAPLUS
DN 142:62766
TI Product of coprecipitation of sparingly soluble substance and water-soluble polymer and process for producing the same
IN Ishikura, Toyoaki; Udagawa, Chikako; Misaka, Masato; Suemune,

Kenji; Kitahara, Shinichi; Ono, Kiyoko; Koyanagi, Akihiro
 PA Meiji Seika Kaisha, Ltd., Japan
 SO PCT Int. Appl., 31 pp.
 CODEN: PIXXD2
 DT Patent
 LA Japanese
 FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|----------------|--|----------|-----------------|----------|
| PI | WO 2004113451 | A1 | 20041229 | WO 2004-JP8727 | 20040621 |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| | RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| | EP 1650266 | A1 | 20060426 | EP 2004-746196 | 20040621 |
| | R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | |
| | US 2007167402 | A1 | 20070719 | US 2005-561212 | 20051219 |
| PRAI | JP 2003-175646 | A | 20030620 | | |
| | WO 2004-JP8727 | W | 20040621 | | |

AB Disclosed is a product of the copptn. of 2-(1-isopropoxy-carbonyloxy-2-methylpropyl)-7,8-dimethoxy-4(5H),10-dioxo-2H-1,2,3-triazolo[4,5-c][1]benzoxazepine (I) and a water-soluble polymer. The copptn. product is excellent in solubility and absorbability. Crystalline I and Me cellulose were dissolved in DMSO. The mixture was dropped into an aqueous solution containing Me cellulose to give ppts., which showed a solubility 16.8

µg/mL, as compared to 0.8 µg/mL for crystalline I.

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2004:1154759 CAPLUS

DN 142:76996

TI Manufacture of coprecipitates of water-insoluble substances and water-soluble polymers

IN Chikase, Shigeru; Misaka, Masato; Udagawa, Chikako; Ishikura, Toyooki

PA Meiji Seika Kaisha, Ltd., Japan

SO PCT Int. Appl., 21 pp.

CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---------------|--|----------|-----------------|----------|
| PI | WO 2004113424 | A1 | 20041229 | WO 2004-JP8728 | 20040621 |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| | RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, | | | |

AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
 EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
 SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
 SN, TD, TG

PRAI JP 2003-175646 A 20030620

AB The title coppts. are manufactured by mixing of solns. of the
 water-insol. substances(e.g., medicines) in aqueous organic solvents(e.g.,
 DMSO,
 N,N-DMF) into flowing liquid media mainly containing water, and continuous
 flowing for copptn., whereas the solns. and/or liquid media
 contain the water-soluble polymers(e.g., cellulose).

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s Udagawa Chikako/AU

L13 4 UDAGAWA CHIKAKO/AU

=> dis 113 1-4 bib abs

L13 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2004:1154779 CAPLUS

DN 142:62766

TI Product of coprecipitation of sparingly soluble substance and

water-soluble polymer and process for producing the same

IN Ishikura, Toyooki; Udagawa, Chikako; Misaka, Masato; Suemune,

Kenji; Kitahara, Shinichi; Ono, Kiyoko; Koyanagi, Akihiro

PA Meiji Seika Kaisha, Ltd., Japan

SO PCT Int. Appl., 31 pp.

CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| PI WO 2004113451 | A1 | 20041229 | WO 2004-JP8727 | 20040621 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BF, BH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1650266 | A1 | 20060426 | EP 2004-746196 | 20040621 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |
| US 2007167402 | A1 | 20070719 | US 2005-561212 | 20051219 |
| PRAI JP 2003-175646 | A | 20030620 | | |
| WO 2004-JP8727 | W | 20040621 | | |

AB Disclosed is a product of the copptn. of 2-(1-isopropoxy-carbonyloxy-2-methylpropyl)-7,8-dimethoxy-4(5H),10-dioxo-2H-1,2,3-triazolo[4,5-c][1]benzoxazine (I) and a water-soluble polymer. The copptn. product is excellent in solubility and absorbability. Crystalline I and Me cellulose were dissolved in DMSO. The mixture was dropped into an aqueous solution containing Me cellulose to give ppts., which showed a solubility 16.8 µg/mL, as compared to 0.8 µg/mL for crystalline I.

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2004:1154759 CAPLUS

DN 142:76996

TI Manufacture of coprecipitates of water-insoluble substances and water-soluble polymers

IN Chikase, Shigeru; Misaka, Masato; Udagawa, Chikako; Ishikura, Toyooki

PA Meiji Seika Kaisha, Ltd., Japan

SO PCT Int. Appl., 21 pp.

CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---------------|--|----------|-----------------|----------|
| PI | WO 2004113424 | A1 | 20041229 | WO 2004-JP8728 | 20040621 |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| | RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |

PRAI JP 2003-175646 A 20030620

AB The title coppts. are manufactured by mixing of solns. of the water-insol. substances(e.g., medicines) in aqueous organic solvents(e.g., DMSO, N,N-DMF) into flowing liquid media mainly containing water, and continuous flowing for copptn., whereas the solns. and/or liquid media contain the water-soluble polymers(e.g., cellulose).

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2003:532667 CAPLUS

DN 139:90493

TI Amorphous substance of tricyclic triazolobenzazepine derivative

IN Ishikura, Toyooki; Ishizawa, Takayuki; Suemune, Kenji; Ishiwata, Mayumi; Udagawa, Chikako

PA Meiji Seika Kaisha, Ltd., Japan

SO PCT Int. Appl., 25 pp.

CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---------------|--|----------|-----------------|----------|
| PI | WO 2003055886 | A1 | 20030710 | WO 2002-JP13558 | 20021225 |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2471651 A1 20030710 CA 2002-2471651 20021225
AU 2002367110 A1 20030715 AU 2002-367110 20021225
EP 1466914 A1 20041013 EP 2002-790871 20021225

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

CN 1617872 A 20050518 CN 2002-827547 20021225
US 2005130955 A1 20050616 US 2004-500071 20040625
US 7229985 B2 20070612
PRAI JP 2001-393016 A 20011226
WO 2002-JP13558 W 20021225

AB Disclosed are amorphous 2-(1-isopropoxycarbonyloxy-2-methylpropyl)-7,8-dimethoxy-4(5H),10-dioxo-2H-1,2,3-triazolo[4,5-c][1]benzazepine (I), which is improved in absorbability and solubility; and a medicinal composition containing the compound. Also provided are processes for producing amorphous compound I and for producing a medicinal composition containing the compound. An amorphous compound I was dissolved in methylene chloride, and mixed with Me cellulose (Metolose SM15) and methanol. The mixture was then spray dried to obtain an amorphous powder of the present invention.

RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1995:995242 CAPLUS
DN 124:57124
TI Double-stranded derivative of polyoxyethylene-containing lipid and its preparation
IN Watanabe, Hiroshi; Taniguchi, Kumi; Udagawa, Chikako; Ando, Takashi; Nakabayashi, Satoru
PA Meiji Seika K. K., Japan
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 9525764 | A1 | 19950928 | WO 1995-JP535 | 19950323 |
| W: JP, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| JP 3631755 | B2 | 20050323 | JP 1995-524546 | 19950323 |
| US 5786387 | A | 19980728 | US 1996-553601 | 19960125 |
| PRAI JP 1994-52181 | A | 19940323 | | |
| JP 1994-302165 | A | 19941206 | | |
| WO 1995-JP535 | W | 19950323 | | |

AB The title lipid useful as drug delivery system or emulsifier is polyethylene glycol bearing long-chain branching group on 1 end. Thus, mixing 100 mg 2-cetyloctadecanoic acid with 39 mg 1,1'-carbonyldiimidazole in 1 mL THF at 70° for 1 h, adding 132 mg α -hydroxy- ω -methylpolyoxyethylene dissolved in 1 mL THF containing catalytic amount of NaOEt, and mixing overnight at 70° gave α -(2-cetyloctadecanoyl)- ω -methylpolyoxyethylene.

=> dis 114 1-3 bib abs

L14 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2004:1154779 CAPLUS
 DN 142:62766
 TI Product of coprecipitation of sparingly soluble substance and
 water-soluble polymer and process for producing the same
 IN Ishikura, Toyooki; Udagawa, Chikako; Misaka, Masato; Suemune,
 Kenji; Kitahara, Shinichi; Ono, Kiyoko; Koyanagi, Akihiro
 PA Meiji Seika Kaisha, Ltd., Japan
 SO PCT Int. Appl., 31 pp.
 CODEN: PIXXD2
 DT Patent
 LA Japanese
 FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| PI | WO 2004113451 | A1 | 20041229 | WO 2004-JP8727 | 20040621 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | EP 1650266 | A1 | 20060426 | EP 2004-746196 | 20040621 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |
| | US 2007167402 | A1 | 20070719 | US 2005-561212 | 20051219 |
| PRAI | JP 2003-175646 | A | 20030620 | | |
| | WO 2004-JP8727 | W | 20040621 | | |

AB Disclosed is a product of the copptn. of 2-(1-isopropoxy-carbonyloxy-2-methylpropyl)-7,8-dimethoxy-4(5H),10-dioxo-2H-1,2,3-triazolo[4,5-c][1]benzoozepine (I) and a water-soluble polymer. The copptn. product is excellent in solubility and absorbability. Crystalline I and Me cellulose were dissolved in DMSO. The mixture was dissolved into an aqueous solution containing Me cellulose to give ppts., which showed a solubility 16.8 µg/mL, as compared to 0.8 µg/mL for crystalline I.

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2004:1154759 CAPLUS
 DN 142:76996
 TI Manufacture of coprecipitates of water-insoluble substances and
 water-soluble polymers
 IN Chikase, Shigeru; Misaka, Masato; Udagawa, Chikako; Ishikura,
 Toyooki
 PA Meiji Seika Kaisha, Ltd., Japan
 SO PCT Int. Appl., 21 pp.
 CODEN: PIXXD2
 DT Patent
 LA Japanese
 FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------------|------|------|-----------------|------|
|--|------------|------|------|-----------------|------|

PI WO 2004113424 A1 20041229 WO 2004-JP8728 20040621
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI JP 2003-175646 A 20030620
AB The title coppts. are manufactured by mixing of solns. of the water-insol. substances(e.g., medicines) in aqueous organic solvents(e.g., DMSO, N,N-DMF) into flowing liquid media mainly containing water, and continuous flowing for copptn., whereas the solns. and/or liquid media contain the water-soluble polymers(e.g., cellulose).
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2008 ACS on SIN
AN 1992:439877 CAPLUS
DN 117:39877
TI The effect of ME1207, a new oral cephalosporin, on the intestinal microflora of beagle dogs
AU Tamura, Atsushi; Ida, Takashi; Saito, Sakiko; Suzuki, Heiji; Niizato, Tetsutaro; Misaka, Masato; Nakayama, Etsuko; Wada, Koichi
CS Pharm. Res. Cent., Meiji Seika Kaisha, Ltd., Yokohama, 222, Japan
SO Chemotherapy (Tokyo) (1992), 40(Suppl. 2), 65-74
CODEN: NKRZAZ; ISSN: 0009-3165
DT Journal
LA Japanese
AB ME1207 (pivaloyloxymethyl ester of ME1206) was orally administered to beagle dogs at 12 mg/kg/day or 250 mg/kg/day for 14 consecutive days. The feces of each group were normal during the experiment, and no changes such as diarrhea were observed. A slight decrease of Enterobacteriaceae and a transient decrease of anaerobes were observed in the 12 mg/kg/day group. A substantial decrease of Enterobacteriaceae was observed and as a result, the main fecal flora was Enterococcus spp. in the 250 mg/kg/day group. The detection rate of Clostridium difficile was high in the 12 mg/kg/day group. The concentration of ME1206 in the feces was low in the 12 mg/kg/day group but high (≥ 1000 $\mu\text{g/g}$) in the 250 mg/kg/day group. β -Lactamase activity in the feces was low. The resistant strains were observed in the Enterobacteriaceae but not in the Staphylococcus spp. during administration of ME1207.

=> s Suemune Kenji/AU
L15 15 SUEMUNE KENJI/AU
=> s l15 and coprecipi?
6856 COPRECIP1?
2591 COPPT
1482 COPPTS
3609 COPPT
(COPPT OR COPPTS)
6440 COPPTD
1034 COPPTG

17317 COPPTN
 61 COPPTNS
 17339 COPPTN
 (COPPTN OR COPPTNS)
 25837 COPRECIPI?
 (COPRECIPI? OR COPPT OR COPPTD OR COPPTG OR COPPTN)
 L16 1 L15 AND COPRECIPI?

=> dis l16 bib abs

L16 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on SIN
 AN 2004:1154779 CAPLUS
 DN 142:62766

TI Product of coprecipitation of sparingly soluble substance and
 water-soluble polymer and process for producing the same
 IN Ishikura, Toyooki; Udagawa, Chikako; Misaka, Masato; Suemune,
 Kenji; Kitahara, Shinichi; Ono, Kiyoko; Koyanagi, Akihiro
 PA Meiji Seika Kaisha, Ltd., Japan
 SO PCT Int. Appl., 31 pp.
 CODEN: PIXXD2
 DT Patent
 LA Japanese
 FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| PI | WO 2004113451 | A1 | 20041229 | WO 2004-JP8727 | 20040621 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | EP 1650266 | A1 | 20060426 | EP 2004-746196 | 20040621 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |
| | US 2007167402 | A1 | 20070719 | US 2005-561212 | 20051219 |
| PRAI | JP 2003-175646 | A | 20030620 | | |
| | WO 2004-JP8727 | W | 20040621 | | |

AB Disclosed is a product of the copptn. of 2-(1-isopropoxy-carbonyloxy-2-methylpropyl)-7,8-dimethoxy-4(5H),10-dioxo-2H-1,2,3-triazolo[4,5-c][1]benzoxazepine (I) and a water-soluble polymer. The copptn. product is excellent in solubility and absorbability. Crystalline I and Me cellulose were dissolved in DMSO. The mixture was dropped into an aqueous solution containing Me cellulose to give ppts., which showed a solubility 16.8 µg/mL, as compared to 0.8 µg/mL for crystalline I.

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s Kitahara Shinichi/AU
 L17 26 KITAHARA SHINICHI/AU

=> s l17 and coprecip?
 6863 COPRECIPI?
 2591 COPPT

1482 COPPTS
 3609 COPPT
 (COPPT OR COPPTS)
 6440 COPPTD
 1034 COPPTG
 17317 COPPTN
 61 COPPTNS
 17339 COPPTN
 (COPPTN OR COPPTNS)
 25841 COPRECIP?
 (COPRECIP? OR COPPT OR COPPTD OR COPPTG OR COPPTN)
 L18 1 L17 AND COPRECIP?

=> dis l18 bib abs

L18 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2004:1154779 CAPLUS

DN 142:62766

TI Product of coprecipitation of sparingly soluble substance and
 water-soluble polymer and process for producing the same
 IN Ishikura, Toyooki; Udagawa, Chikako; Misaka, Masato; Suemune, Kenji;
 Kitahara, Shinichi; Ono, Kiyoko; Koyanagi, Akihiro
 PA Meiji Seika Kaisha, Ltd., Japan
 SO PCT Int. Appl., 31 pp.
 CODEN: PIXXD2

DT Patent
 LA Japanese
 FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--------|---|---|----------|-----------------|----------|
| PI | WO 2004113451 | A1 | 20041229 | WO 2004-JP8727 | 20040621 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | EP 1650266 | A1 | 20060426 | EP 2004-746196 | 20040621 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |
| | US 2007167402 | A1 | 20070719 | US 2005-561212 | 20051219 |
| PRAI | WO 2003-175646 | A | 20030620 | | |
| | WO 2004-JP8727 | W | 20040621 | | |
| AB | Disclosed is a product of the copptn. of 2-(1-isopropoxy-carbonyloxy-2-methylpropyl)-7,8-dimethoxy-4(5H),10-dioxo-2H-1,2,3-triazolo[4,5-c][1]benzoxazine (I) and a water-soluble polymer. The copptn. product is excellent in solubility and absorbability. Crystalline I and Me cellulose were dissolved in DMSO. The mixture was dropped into an aqueous solution containing Me cellulose to give ppts., which showed a solubility 16.8 | | | | |
| | μg/mL, as compared to 0.8 μg/mL for crystalline I. | | | | |
| RE.CNT | 15 | THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT | | | |

=> s Ono Kiyoko/AU

=> dis 119 1-5 bib abs

L19 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2005:1078892 CAPLUS
 DN 144:104441
 TI Stereoselectivity of the reduced folate carrier in Caco-2 cells
 AU Narawa, Tomoya; Shimizu, Rikako; Takano, Shuhei; Tsuda, Yasuyuki;
 Ono, Kiyoko; Yamada, Hideo; Itoh, Tomoo
 CS School of Pharmaceutical Sciences, Kitasato University, Tokyo, Japan
 SO Chirality (2005), 17(8), 444-449
 CODEN: CHRLEP; ISSN: 0899-0042
 PB Wiley-Liss, Inc.
 DT Journal
 LA English
 AB Stereoselectivity of the human reduced folate carrier (RFC1) was examined in Caco-2 cells using methotrexate (L-amethopterin or L-MTX) and its antipode (D-amethopterin or D-MTX) as model substrates. The initial uptake rate of folic acid (FA) was concentration-dependent, with a Km value of approx. 0.6 μ M. The Eadie-Hofstee plot of the RFC1-mediated FA uptake revealed a single component for FA uptake into Caco-2 cells, demonstrating that only RFC1 is involved in FA uptake. L-MTX inhibited FA uptake in a competitive manner with a Ki value of approx. 2 μ M, similar to the Km value of L-MTX. D-MTX also competitively inhibited FA uptake with a Ki value being approx. 120 μ M, indicating that the affinity of D-MTX is approx.60-fold less than that of L-MTX. The stereoselectivity of human RFC1 observed in the present study was consistent not only with the stereoselectivity of rabbit RFC1 observed in rabbit intestinal brush border membrane vesicles but also with the reported differences in oral absorption of amethopterin enantiomers in humans.

RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2004:1154779 CAPLUS
 DN 142:62766
 TI Product of coprecipitation of sparingly soluble substance and water-soluble polymer and process for producing the same
 IN Ishikura, Toyooki; Udagawa, Chikako; Misaka, Masato; Suemune, Kenji; Kitahara, Shinichi; Ono, Kiyoko; Koyanagi, Akihiro
 PA Meiji Seika Kaisha, Ltd., Japan
 SO PCT Int. Appl., 31 pp.
 CODEN: PIXXD2
 DT Patent
 LA Japanese
 FAN.CNT 2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------|--|----------|-----------------|----------|
| PI WO 2004113451 | A1 | 20041229 | WO 2004-JP8727 | 20040621 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |

EP 1650266 A1 20060426 EP 2004-746196 20040621
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
 US 2007167402 A1 20070719 US 2005-561212 20051219
 PRAI JP 2003-175646 A 20030620
 WO 2004-JP8727 W 20040621

AB Disclosed is a product of the copptn. of 2-(1-isopropoxy-carbonyloxy-2-methylpropyl)-7,8-dimethoxy-4(5H),10-dioxo-2H-1,2,3-triazolo[4,5-c][1]benzoozepine (I) and a water-soluble polymer. The copptn. product is excellent in solubility and absorbability. Crystalline I and Me cellulose were dissolved in DMSO. The mixture was dropped into an aqueous solution containing Me cellulose to give ppts., which showed a solubility 16.8 µg/mL, as compared to 0.8 µg/mL for crystalline I.

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 2001:146120 CAPLUS
 DN 134:320497
 TI Stereoselectivity of the folate transporter in rabbit small intestine: studies with amethopterin enantiomers
 AU Itoh, Tomoo; Ono, Kiyoko; Koido, Kei-Ichi; Li, Yin-Hua; Yamada, Hideo
 CS Department of Pharmaceuticals, School of Pharmaceutical Sciences, Kitasato University, Tokyo, 108-8641, Japan
 SO Chirality (2001), 13(3), 164-169
 CODEN: CHRLEP; ISSN: 0899-0042
 PB Wiley-Liss, Inc.
 DT Journal
 LA English
 AB Stereoselectivity of the folate transporter was examined using rabbit intestinal brush border membrane vesicles (BBMV). Methotrexate (MTX) and the antipode (D-amethopterin) were used as model substrates of the transporter. Folic acid (FA) and MTX were actively taken up into BBMV in the presence of an H⁺ gradient. Initial uptake of FA and MTX was concentration-dependent with Km values of 1.5 and 1.6 µM for FA and MTX, resp. FA and MTX mutually inhibited uptake in a competitive manner, with Ki values being similar to the corresponding Km values, demonstrating that FA and MTX share the folate transporter. D-Amethopterin also inhibited FA uptake competitively, with a Ki value approx. 60-fold greater than that of MTX, showing that the affinity of the D-isomer (D-amethopterin) to the folate transporter is much less than that of the L-isomer (MTX). The extent of stereoselectivity observed in the present study is consistent with the previously reported differences in plasma concentration between amethopterin enantiomers following oral administration in humans.

RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 1988:610541 CAPLUS
 DN 109:210541
 TI process for the preparation of pyruvic acid or its esters from methacrylic acid or its esters
 IN Arashiba, Nobumasa; Asano, Shiro; Ono, Kiyoko
 PA Mitsui Toatsu Chemicals, Inc., Japan
 SO Jpn. Kokai Tokkyo Koho, 5 pp.
 CODEN: JKXXAF
 DT Patent
 LA Japanese

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|----------------|------|----------|-----------------|----------|
| PI | JP 63126840 | A | 19880530 | JP 1986-272807 | 19861118 |
| PRAI | JP 1986-272807 | | 19861118 | | |

OS CASREACT 109:210541

AB Pyruvic acid (I) or its esters are prepared by O3-oxidation of methacrylic acid (II) or its esters, followed by hydrogenation of the resulting reaction mixture in the presence of Pd at $\leq 15^\circ$. A solution of II in MeOH was bubbled with O3-containing O between -15 and -20° for 70 min and the reaction mixture was treated with Pd/C with feeding of H between -5 and -10° for 30 min to give 97% I (conversion 100%), vs. 1% (conversion 100%) for a control by hydrogenation at $17-20^\circ$.

L19 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

AN 1988:437513 CAPLUS

DN 109:37513

TI Process for the preparation of glyoxylic acid useful as intermediates for pharmaceuticals and agrochemicals

IN Arashiba, Nobumasa; Asano, Shiro; Ono, Kiyoko

PA Mitsui Toatsu Chemicals, Inc., Japan

SO Jpn. Kokai Tokkyo Koho, 6 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|----------------|------|----------|-----------------|----------|
| PI | JP 62298552 | A | 19871225 | JP 1986-139211 | 19860617 |
| PRAI | JP 1986-139211 | | 19860617 | | |

OS CASREACT 109:37513

AB Glyoxylic acid (I), a known intermediate for pharmaceuticals, agrochems., cosmetics, and perfumes, is prepared from maleic acid (II) with high selectivity and yield. To II dissolved in MeOH at -45 to -40° , was fed 0.93 volume% O3 in O2 for 2 h followed by N for 15 min and then the reaction mixture was stirred at 10 kg/cm2 H gage in the presence of 52 weight% Pd/Al2O3 to heat slowly up to 10° in 1.5 h and for further 1 h at 10° to give 93% I (II conversion at 100%) without peroxide formation.

=> s Koyanagi Akihiro/AU

L20 7 KOYANAGI AKIHIRO/AU

=> dis 120 1-7 bib abs

L20 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2006:156927 CAPLUS

DN 144:403759

TI Tricyclic pharmacophore-based molecules as novel integrin $\alpha v\beta 3$ antagonists. Part 2: Synthesis of potent $\alpha v\beta 3/\alpha IIb\beta 3$ dual antagonists

AU Ishikawa, Minoru; Kubota, Dai; Yamamoto, Mikio; Kuroda, Chizuko; Iguchi, Maki; Koyanagi, Akihiro; Murakami, Shoichi; Ajito, Keiichi

CS Pharmaceutical Research Department, Meiji Seika Kaisha, Ltd., Yokohama, 222-8567, Japan

SO Bioorganic & Medicinal Chemistry (2006), 14(7), 2109-2130

CODEN: BMECEP; ISSN: 0968-0896

PB Elsevier B.V.

DT Journal

LA English

AB We synthesized 4-aminopiperidine derivs. of our prototype integrin $\alpha v\beta 3$ antagonist 1 in an attempt to increase the activity and water solubility. Introduction of one or two hydrophilic moieties into the central aromatic ring and/or the benzene ring at the C-terminus of 1 increased water solubility and enhanced inhibition of cell adhesion. The results of a structure-activity relationships (SAR) study indicated that the torsion angle between the central aromatic ring and the piperidine ring, and the acidity at the sulfonamide moiety, might be important for $\alpha v\beta 3$ receptor binding activity. Some of these compds. are novel and potent $\alpha v\beta 3/\alpha IIb\beta 3$ dual antagonists with acceptable water solubility and a satisfactory early absorption, distribution, metabolism, excretion, and toxicity (ADMET) profile.

RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2004:1154779 CAPLUS

DN 142:62766

TI Product of coprecipitation of sparingly soluble substance and water-soluble polymer and process for producing the same

IN Ishikura, Toyooki; Udagawa, Chikako; Misaka, Masato; Suemune, Kenji; Kitahara, Shinichi; Ono, Kiyoko; Koyanagi, Akihiro

PA Meiji Seika Kaisha, Ltd., Japan

SO PCT Int. Appl., 31 pp.

CODEN: PIXXD2

DT Patent

LA Japanese

FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|---|------|----------|-----------------|----------|
| PI | WO 2004113451 | A1 | 20041229 | WO 2004-JP8727 | 20040621 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | EP 1650266 | A1 | 20060426 | EP 2004-746196 | 20040621 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |
| | US 2007167402 | A1 | 20070719 | US 2005-561212 | 20051219 |
| | PRAI JP 2003-175646 | A | 20030620 | | |
| | WO 2004-JP8727 | W | 20040621 | | |

AB Disclosed is a product of the copptn. of 2-(1-isopropoxy-carbonyloxy-2-methylpropyl)-7,8-dimethoxy-4(5H),10-dioxo-2H-1,2,3-triazolo[4,5-c][1,1benzoozepine (I) and a water-soluble polymer. The copptn. product is excellent in solubility and absorbability. Crystalline I and Me cellulose were dissolved in DMSO. The mixture was dropped into an aqueous solution containing Me cellulose to give ppts., which showed a solubility 16.8 $\mu\text{g/mL}$, as compared to 0.8 $\mu\text{g/mL}$ for crystalline I.

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L20 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN

AN 2001:695818 CAPLUS

DN 136:363213
 TI Role of transporter and metabolic enzyme in sequential and competitive process of intestinal absorption: Study on SGLT1, disaccharidase and peptidases
 AU Mizuma, Takashi; Matsumoto, Seichi; Hagi, Katsura; Koyanagi, Akihiro; Narasaka, Takuo; Fuseda, Norihiko; Hayashi, Masahiro; Awazu, Shoji
 CS Department of Biopharmaceutics, School of Pharmacy, Tokyo University of Pharmacy and Life Science, Hachioji, Tokyo, Japan
 SO Yakubutsu Dotai (2001), 16(3), 258-263
 CODEN: YADOEL; ISSN: 0916-1139
 PB Nippon Yakubutsu Dotai Gakkai
 DT Journal
 LA Japanese
 AB We have studied intestinal metabolism and transport, which is considered to be a sequential (1) or competitive (2) process in absorption (Scheme 1). (1) Disaccharide (maltose, cellobiose, lactose) conjugates of p-nitrophenol were hydrolyzed to p-nitrophenyl β -glucosides (p-NP β glc) on the mucosal side. The p-NP β glc was transported by Na⁺/glucose cotransporter (SGLT1). Transport clearance of p-NP β glc formed from cellobiose and lactose conjugates of p-NP were higher than that from maltose or of p-NP β glc itself. These results suggest that SGLT1 is cooperatively coupled with lactase/phloridzin hydrolase catalyzing hydrolysis of cellobiose and lactose conjugates. There might be a cooperative relationship between peptidase and H⁺/oligopeptide cotransporter or amino acid transporter as well. (2) Kyotorphin (KTP) was too unstable in intestine to be absorbed. KTP appeared on the serosal side in the presence of peptidase inhibitors. Meanwhile, cyclic KTP was stable in intestine to be absorbed. Absorption clearance of cyclic KTP was higher than the overall transport clearance of KTP, which was calculated according to the metabolic inhibition model. Competitive process was observed in intestinal absorption of α -naphthol as well. These results indicate that metabolism degradation and membrane transport are competitive. Unless a drug is stabilized against metabolic enzyme, intestinal absorption of the drug can not be improved even if membrane transport is increased.

L20 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2008 ACS on SIN
 AN 2001:311798 CAPLUS
 DN 135:252146

TI Critical factor in intestinal absorption of peptide drugs: Quantitative analysis of peptide drug absorption which is competitive process of metabolism and transport
 AU Mizuma, Takashi; Koyanagi, Akihiro; Awazu, Shoji
 CS Department of Biopharmaceutics, Tokyo Yakka University, Tokyo, Japan
 SO Peptide Science (2001), Volume Date 2000, 37th, 259-262
 CODEN: PSCIFQ; ISSN: 1344-7661
 PB Japanese Peptide Society
 DT Journal
 LA English
 AB Intestinal absorption of modified kyotorphin (KTP) analogs were kinetically evaluated. Absorption clearance (CLabs) of cyclic KTP, KTP-pAPP β glc and Boc-KTP-pAPP β glc were higher than that of KTP (0.247 μ l/min/cm) indicating that derivatization of KTP increases the membrane permeability. Furthermore, the greater the metabolic clearance (CLmet) of KTP and its derivs., the lower the CLabs. These results and simulation study led to the conclusion that intestinal absorption of peptide drugs is a competitive process of metabolism and transport and that metabolic degradation in the intestinal tissues is more critical than membrane permeability (transport) for oral delivery of peptide drugs.

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

- L20 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 1997:191199 CAPLUS
 DN 126:287519
 TI Intestinal transport and metabolism of analgesic dipeptide, kyotorphin: rate-limiting factor in intestinal absorption of peptide as drug
 AU Mizuma, Takashi; Koyanagi, Akihiro; Awazu, Shoji
 CS Department of Biopharmaceutics, School of Pharmacy, Tokyo University of Pharmacy and Life Science, 1432-1 Horinouchi, Hachioji, Tokyo, 192-03, Japan
 SO Biochimica et Biophysica Acta, General Subjects (1997), 1335(1-2), 111-119
 CODEN: BBGSB3; ISSN: 0304-4165
 PB Elsevier B.V.
 DT Journal
 LA English
 AB Intestinal transport and metabolism of kyotorphin (KTP) were studied in rat everted small intestine. KTP on the mucosal side was metabolized completely within 60 min, and any amts. of KTP were not detected on the serosal side. On the other hand, [D-Arg2]-KTP (D-KTP) was stable on the mucosal side to appear on the serosal side. However, N-t-butoxycarbonyl-KTP (Boc-KTP), which was metabolized on the mucosal side faster than KTP, appeared on the serosal side. In intestinal homogenate, KTP was metabolized, and the metabolic clearance (CL_{met}) was decreased by peptidase inhibitors, bestatin, o-phenanthroline and tryptophan hydroxamate. In the presence of these peptidase inhibitors, the absorption clearance (CL_{abs}) of KTP was increased. The less the CL_{met} of KTP was, the more the CL_{abs} of KTP was. Meanwhile, Boc-KTP in intestinal homogenate was stable even in the absence of peptidase inhibitors. The CL_{abs} of Boc-KTP was constant irres. of the stability on the mucosal side. Kinetic anal. by the metabolic inhibition model indicated that the stabilization of KTP in the intestinal tissue could increase the CL_{abs} up to 0.247 $\mu\text{L}/\text{min per cm}$, which was as much as the CL_{abs} of stable D-KTP. These results led to the conclusion that rate-limiting process in intestinal absorption of KTP is metabolic degradation in intestinal tissue during the absorption.
- L20 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN
 AN 1996:417940 CAPLUS
 DN 125:123422
 TI Improvement of intestinal absorption of leucine enkephalin by sugar coupling and peptidase inhibitors
 AU Mizuma, Takashi; Ohta, Kunihiro; Koyanagi, Akihiro; Awazux, Shoji
 CS School of Pharmacy, Tokyo University of Pharmacy and Life Science, Tokyo, 192-03, Japan
 SO Journal of Pharmaceutical Sciences (1996), 85(8), 854-857
 CODEN: JPMSAE; ISSN: 0022-3549
 PB American Chemical Society
 DT Journal
 LA English
 AB Peptidase-degradable leucine enkephalin (LE) was coupled with cellobiose or gentiobiose. In the absorption expts., cellobiose-coupled LE (CcPLE) was more stable than LE itself on the mucosal side, and CcPLE appeared on the serosal side. Destyrosyl LE coupled with cellobiose was not formed, indicating that sugar coupling provided LE with aminopeptidase resistance. In the presence of angiotensin-converting enzyme and enkephalinase inhibitors, the stability of CcPLE on the mucosal side was increased, and as a result more was absorbed. Furthermore, the absorption clearance was much higher than the value expected from the mucosal concentration of CcPLE. Similar results were observed in the absorption of gentiobiose-coupled LE.

In the LE absorption experiment, however, LE was not detected on the serosal side even in the presence of these peptidase inhibitors. Improvement of intestinal absorption by sugar coupling and peptidase inhibitors was evaluated kinetically, indicating the exclusive contribution of metabolic degradation of LE through intestinal tissues to the absorption process.

L20 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2008 ACS on STN

AN 1988:86086 CAPLUS

DN 108:86086

TI Preparation of superconductive specimens in yttrium-barium-copper-oxygen system by coprecipitation method

AU Koyanagi, Akihiro; Ohta, Joji; Koizumi, Hirokazu; Suzuki, Takayoshi

CS Inst. Ind. Sci., Univ. Tokyo, Tokyo, 106, Japan

SO Seisan Kenkyu (1987), 39(11), 454-5

CODEN: SEKEAI; ISSN: 0037-105X

DT Journal

LA Japanese

AB To an aqueous solution containing $\text{Cu}(\text{NO}_3)_2$, $\text{Y}(\text{NO}_3)_3$, and $\text{Ba}(\text{NO}_3)_2$ in the molar ratio

of $\text{Y}(\text{III}):\text{Ba}(\text{II}):\text{Cu}(\text{II})$ of 1:2:3 was added an aqueous solution containing K oxalate,

followed by adjustment of the pH to neutral or alkaline, to obtain coppt. of $\text{Cu}(\text{C}_2\text{O}_4)$, $\text{Y}_2(\text{C}_2\text{O}_4)_3$, and $\text{Ba}(\text{C}_2\text{O}_4)$. The coppt. was pyrolyzed at 750° and finally sintered at 950° in air for 12 h.

Measurements of the d.c. conductivity of the resulting sintered body showed a transition to supercond. at 91-5% with a narrower transition temperature range and higher critical elec. c.d. as compared with a sintered body made from Y_2O_3 , BaCO_3 , and CuO powders. The sintered body prepared by the copptn. method was composed of fine (1-2)- μm grains.